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Application No.: 10/748010

Case No.: 58281US004

#### Amendments to the Claims:

The following Listing of Claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims**

### What is Claimed is:

- 1. (Currently amended) An immunostimulatory combination comprising:
  - a Toll-Like Receptor (TLR) agonist; and
  - a TNF/R CD40 agonist or a 4-1BB agonist;

each in an amount that, in combination with the other, is effective to <u>produce a synergistic</u> increase <u>in</u> a subject's immune response to an antigen.

- 2. (Original) The immunostimulatory combination of claim 1 wherein the TLR agonist is an agonist of at least one of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, or any combination of any of the foregoing.
- 3. (Currently amended) The immunostimulatory combination of claim 2 wherein the TLR agonist comprises an <u>immune response modifier (IRM)</u> compound or an agonist of TLR2.
- 4. (Currently amended) The immunostimulatory combination of claim 1 wherein the TLR agonist comprises an IRM compound, MALP-2, <u>Pam3cys</u>, <u>LPS</u>, polyIC, CpG, or any combination of any of the foregoing.
- 5. (Currently amended) The immunostimulatory combination of claim 1 wherein the TLR agonist 3 wherein the IRM compound comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, a thiazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.

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- 6. (Withdrawn) The immunostimulatory combination of claim 1 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.
- 7. (Withdrawn) The immunostimulatory combination of claim 6 wherein the TNF/R agonist comprises an agonist of CD40 ligand, OX40 ligand, 4-1BB ligand, CD27, CD30 ligand (CD153), TNF-α, TNF-β, RANK ligand, LT-α, LT-β, GITR ligand, or LIGHT
- 8. (Currently amended) The immunostimulatory combination of claim 1 wherein the <u>4-</u>
  1BB TNF/R agonist comprises an agonist of a TNFR Superfamily member agonistic antibody.
- 9. (Currently amended) The immunostimulatory combination of claim 1 8 wherein the TNF/R CD40 agonist comprises an anti-CD40 antibody or a receptor binding domain of CD40 ligand. an agonist of CD40, OX40, 4 1BB, CD70 (CD27 ligand), CD30, TNFR2, RANK, LT-BR, HVEM, GITR, TROY, or RELT.
- 10. (Currently amended) The immunostimulatory combination of claim 1 wherein the TNF/R CD40 agonist comprises an agonistic antibody.
- 11. (Withdrawn) A method of inducing a T<sub>H</sub>1 immune response in a subject comprising: co-administering to the subject a TLR agonist and a TNF/R agonist, each in an amount that, when in combination with the other, is effective to induce a T<sub>H</sub>1 immune response.
- 12. (Withdrawn) The method of claim 11 wherein the TLR agonist comprises an agonist of TLR2.
- 13. (Withdrawn) The method of claim 11 wherein the TLR agonist comprises an agonist of TLR9.

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- 14. (Withdrawn) The method of claim 11 wherein the TLR agonist comprises an agonist of TLR8.
- 15. (Withdrawn) The method of claim 11 wherein the TLR agonist comprises an agonist of TLR7.
- 16. (Withdrawn) The method of claim 11 further comprising co-administering an antigen in an amount effective to induce an immune response in the subject.
- 17. (Withdrawn) A method of activating antigen-specific CD8<sup>+</sup> T cells in a subject comprising:

co-administering to the subject a TLR agonist and a TNF/R agonist, each in an amount that, in combination with the other, is effective to activate antigen-specific CD8<sup>+</sup> T cells.

- 18. (Withdrawn) The method of claim 17 further comprising co-administering an antigen in an amount effective to induce an immune response in the subject.
- 19. (Withdrawn) The method of claim 17 wherein activating CD8<sup>+</sup> T cells comprises expansion of CD8<sup>+</sup> effector T cells.
- 20. (Withdrawn) The method of claim 17 wherein activating CD8<sup>+</sup> T cells comprises generating CD8<sup>+</sup> memory T cells.
- 21. (Withdrawn) The method of claim 17 wherein the TLR agonist comprises an agonist of TLR2.
- 22. (Withdrawn) The method of claim 17 wherein the TLR agonist comprises an agonist of TLR9.

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- 23. (Withdrawn) The method of claim 17 wherein the TLR agonist comprises an agonist of TLR8.
- 24. (Withdrawn) The method of claim 17 wherein the TLR agonist comprises an agonist of TLR7.
- 25. (Withdrawn) The method of claim 17 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.
- 26. (Withdrawn) The method of claim 17 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.
- 27. (Withdrawn) The method of claim 17 wherein the TNF/R agonist comprises an agonistic antibody.
- 28. (Withdrawn) A method of activating antigen-specific memory CD8<sup>+</sup> T cells in a subject having prior exposure to an antigen, comprising:

administering to the subject the antigen in an amount effective to induce antigen-specific CD8<sup>+</sup> memory T cells to become activated, thereby generating antigen-specific CD8<sup>+</sup> effector T cells.

- 29. (Withdrawn) The method of claim 28 further comprising co-administering a TLR agonist in an amount effective to induce antigen-specific CD8<sup>+</sup> memory T cells to become activated, thereby generating antigen-specific CD8<sup>+</sup> effector T cells.
- (Withdrawn) The method of claim 28 wherein the TLR agonist comprises an agonist of TLR2.
- 31. (Withdrawn) The method of claim 28 wherein the TLR agonist comprises an agonist of TLR9.

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- 32. (Withdrawn) The method of claim 28 wherein the TLR agonist comprises an agonist of TLR8.
- 33. (Withdrawn) The method of claim 28 wherein the TLR agonist comprises an agonist of TLR7.
- 34. (Withdrawn) A method of treating a condition in a subject comprising:

  co-administering to the subject a TLR agonist and a TNF/R agonist, each administered in
  an amount that, when in combination with the other, is effective for stimulating a cell-mediated
  immune response.
- 35. (Withdrawn) The method of claim 34 wherein the TLR agonist comprises an agonist of TLR2.
- 36. (Withdrawn) The method of claim 34 wherein the TLR agonist comprises an agonist of TLR9.
- 37. (Withdrawn) The method of claim 34 wherein the TLR agonist comprises an agonist of TLR8.
- 38. (Withdrawn) The method of claim 34 wherein the TLR agonist comprises an agonist of TLR7.
- 39. (Withdrawn) The method of claim 34 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.
- 40. (Withdrawn) The method of claim 34 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.

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- 41. (Withdrawn) The method of claim 34 wherein the TNF/R agonist comprises an agonistic antibody.
- 42. (Withdrawn) The method of claim 34 further comprising co-administering an antigen associated with the condition in an amount effective for inducing a cell-mediated immune response.
- 43. (Withdrawn) The method of claim 34 wherein the condition comprises a neoplastic disease.
- 44. (Withdrawn) The method of claim 43 wherein co-administering the TLR agonist and the TNF/R agonist provides prophylactic treatment.
- 45. (Withdrawn) The method of claim 43 wherein co-administering the TLR agonist and the TNF/R agonist provides therapeutic treatment.
- 46. (Withdrawn) The method of claim 34 wherein the condition comprises an infectious disease.
- 47. (Withdrawn) The method of claim 46 wherein co-administering the TLR agonist and the TNF/R agonist provides prophylactic treatment.
- 48. (Withdrawn) The method of claim 46 wherein co-administering the TLR agonist and the TNF/R agonist provides therapeutic treatment.
- 49. (Currently amended) A vaccine comprising:
  - a TLR agonist;
  - a TNF/R CD40 agonist or a 4-1BB agonist; and an antigen;

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each in an amount that, in combination with the others, is effective for inducing an a synergistic immune response to the antigen in a subject immunized with the vaccine.

- 50. (Withdrawn) The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR2.
- 51. (Withdrawn) The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR9.
- 52. (Withdrawn) The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR8.
- 53. (Original) The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR7.
- 54. (Withdrawn) The vaccine of claim 49 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.
- 55. (Currently amended) The vaccine of claim 49 wherein the TNF/R 4-1BB agonist comprises an agonist of a TNFR Superfamily member agonistic antibody.
- 56. (Currently amended) The vaccine of claim 49 wherein the TNF/R CD40 agonist comprises an agonistic antibody.
- 57. (Original) The vaccine of claim 49 wherein the antigen comprises a tumor antigen, a viral antigen, a bacterial antigen, or a parasitic antigen.